

## REMARKS

The claims are 15-27. The non-elected claims are cancelled without prejudice to applicants' rights thereto.

The objection to the claims based on improper dependency is mooted by the amendment.

The claims are rejected under 35 U.S.C. §112, second paragraph, for several reasons. Reason b), c), d), and e) are mooted by the amendment. Reason a) is traversed. What is meant by "a rapamycin" is not unclear; and the fact that rapamycin is a single compound does not make "a rapamycin" unclear. The expression "a rapamycin" clearly means that a genus of rapamycins is intended. For example, in claim 5, the rapamycin is defined as being either "rapamycin" (the single compound referred to by the Examiner) or "a ... rapamycin" (a genus of rapamycins). There is nothing unclear about the distinction between "rapamycin" and "a rapamycin".

The claims are also rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. The rejection is traversed. Applicants have provided specific examples for producing antibody-producing hybridomas and the supporting literature references. The procedure is described from the starting rapamycin, through the linkages to form immunogenic conjugates, and to the selection of hybridomas selected for the production of high-affinity monoclonal antibodies. Nothing more is necessary to enable one of ordinary skill in the art to reproduce the invention. With regard to the Examiner's objections based on antibodies with different specificities, this problem has been discussed and the solution explained in the specification. The Examiner's attention is directed to the discussion beginning on page 7. Further, the rejection is untenable in view of the rejection under 35 U.S.C. §103, which the Examiner supports by stating (Office Action, page 6): "...well within the level of skill in the art ... with the expectation ... to obtain similarly useful antibodies specific to rapamycin...". Although the rejection is traversed, *infra*, it is clear from the rejection that the Examiner believes that the invention is fully enabled. In view of this belief by the Examiner, the rejection is untenable. It is also noted that in Niwa (cited by the Examiner) there is no reference to a deposited hybridoma.

Claims 1-7, 13, and 14 are rejected under 35 U.S.C. 103 as obvious over a combination of ten references. The rejection is traversed. These references show that rapamycins are known and also that it is known to make antibodies from compounds other than rapamycin. However, the problem with trying to use rapamycins as antigens is that they are immunosuppressive, i.e., the antitheses of the types of compounds from which antibodies would be expected to be raised. Thus,

*contra* to the Examiner's conclusion, one of ordinary skill in the art would not combine these references "with the expectation" of producing rapamycin-specific antibodies. The Examiner's characterization of the rapamycins as "immunogens" is without basis. If the Examiner maintains the rejection, it is requested that the Examiner support the statement that these compounds are known immunogens.


Claims 1-7, 13, and 14 are also rejected under 35 U.S.C. 103 as obvious over the above references and further over Niwa. The rejection is traversed. Rather than support the rejection, Niwa's teaching of antibodies raised against a single compound strongly suggests that it is an extremely narrow teaching from which there should be no expectation of applicability to other compounds. Furthermore, since the mechanisms of immunosuppression are different for the FK506 (tacrolimus, the Niwa compound) and rapamycin, this further limits the teachings of the Niwa reference to its specific compound. Tacrolimus acts at the cellular level by forming a complex which further complexes with calcineurin. However, rapamycin forms no analogous calcineurin complex. Since the mechanisms through which the compounds act are different, there can be no expectation that the teachings of Niwa would be successful when applied to rapamycin.

It is requested that the amendment be entered and that the Examiner reconsider the rejection in view of the amendment and remarks and that the case be passed to issue.

A two-month extension is hereby requested pursuant to 37 CFR §1.136(a) to respond to the Office Action of September 27, 2001. Charge Deposit Account No. 19-0134 in the name of Novartis Corporation in the amount of **\$400** for payment of the extension fee. The Commissioner is hereby authorized to charge any additional fees under 37 CFR §1.17 which may be required, or credit any overpayment, to Account No. 19-0134

Respectfully submitted,

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